Sleeve lobectomy for non-small cell lung cancer and carcinoids: results in 160 cases

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Abstract

Objective: To assess operative mortality (OM), morbidity and long-term results of sleeve lobectomies performed for non-small cell lung cancer (NSCLC) and carcinoids during a 35-year period. Methods: A retrospective review of patients who underwent a sleeve lobectomy for NSCLC and carcinoids was undertaken, univariate and multivariate analyses of factors influencing early mortality in NSCLC were performed and for this purpose the series was split into an early and a contemporary phase, the Kaplan–Meier method was used to calculate the cumulative survival rate, and statistical significance was calculated with the log–rank test. Causes of death were evaluated in relation to the stage of the disease.

Results: OM for NSCLC was 14.6% in the early phase and 6% in the contemporary one; late stenosis occurred in 7.7% of NSCLC patients in the early phase and in 2% in the contemporary one. No OM or late stenosis occurred in carcinoid patients. Three, 5 and 10-year survival rates excluding carcinoids were 77, 62 and 31% for stage I(A–B), 45, 34 and 27% for stage II(A–B), 33, 22 and 0% for stage III(A–B). The 10-year survival rate for carcinoids was 100%. There was no significant difference in long-term survival between stages II and III, while the difference between stage I and stages II and III was significant \( (P < 0.001) \). When survival was analyzed in relation to nodal status, 3, 5 and 10-year survival rates were 71, 57 and 33% for N0 disease, 42, 33 and 22% for N1 disease, and 34 and 19% with the last observation at 82 months of N2 disease; there was no significant difference in survival between N1 and N2 disease. A second primary lung cancer occurred in six patients (3.7%) who underwent resection. Late mortality was not related to cancer in most stage I patients while in stages II and III patients it was related to local and distant recurrences. Conclusions: Sleeve lobectomy is a valid alternative to pneumonectomy: careful patient selection and surgical technique make it possible to achieve a mortality rate comparable to or lower than that for pneumonectomy along with a better quality of life. In addition, it allows further lung resection, if necessary. © 2002 Elsevier Science B.V. All rights reserved.

Keywords: Lung cancer; Sleeve lobectomy

1. Introduction

Since the first sleeve lobectomy for a bronchial carcinoma was reported by Allison [1] in 1954, there have been many reports dealing with the long-term functional [2,3] and oncological results of sleeve lobectomies for the treatment of non-small cell lung cancer (NSCLC). Although sleeve lobectomy for lung cancer was first introduced in clinical practice as an alternative to pneumonectomy for those patients with marked impairment of pulmonary function, it has become apparent that it is not a compromise procedure but is an oncologically adequate procedure with morbidity, mortality and long-term survival rates comparable to those of pneumonectomy [4] but with a better quality of life due to the greater cardiopulmonary reserve. Accordingly, sleeve lobectomy has become the procedure of choice for cancer extending to the orifice of either the right or left upper lobe bronchus and the adjacent main stem bronchus or involving the intermediate or proximal lower lobe bronchus, even in patients with normal pulmonary function. This has allowed the indication to be extended to elderly patients or patients with associated comorbidity factors in whom pneumonectomy would be hazardous.

2. Materials and methods

From 1965 through 1999, 160 patients (147 males and 13 females) with a mean age of 61 years (SD 10.7) and a median age of 63 years underwent a sleeve lobectomy with a full resection of a sleeve of bronchus for a NSCLC or for a carcinoid tumor. Due to the length of this period, preoperative
evaluation changed over time. From 1982 onwards a computerized tomography (CT) scan of the chest, abdomen and brain was included in the preoperative staging. Mediastinoscopy was not routinely performed, but it was performed to exclude N3 disease or more recently to confirm an N2 disease suspected at CT scan before starting induction chemotherapy. A bone scintiscan was obtained in most cases treated from the early 1980s onwards. Functional evaluation included a standard pulmonary function test and, if required, a pulmonary perfusion scan. The stair climbing test was used as a method for functional evaluation for many years before the introduction of the oxygen consumption test to evaluate cardiopulmonary reserve. DLCO has been part of the routine preoperative functional evaluation as a predictor of postoperative complications since 1994. Preoperative findings, either bronchoscopy or CT scan, often identified a possible candidate for a sleeve lobectomy, but of course the final decision to perform a sleeve resection was taken intraoperatively, sometimes after detection by the pathologist in frozen sections of residual tumor on bronchial margins.

Sleeve lobectomy, involved the right upper lobe in 124 cases, the left upper lobe in 19 cases, left lower lobes in ten cases, right upper and middle lobe in four cases and right middle and lower lobe in three cases. It was also performed for peripheral tumors when cancerous invasion of the main bronchus was due to a metastatic N1 node. A functional necessity was present in 36 patients (22.5%), while in 124 patients without respiratory impairment or comorbidity sleeve lobectomy was performed in order to avoid a pneumonectomy. In nine patients (5.6%) an arterioplasty was associated (two arterial sleeve resections and seven tangential arterial resections) and in two patients a chest wall resection was performed. Systemic lymph node dissection was carried out in almost all patients. An incomplete resection was carried out in seven patients (six for R1 on bronchial margin, one for R1 on bronchial margin and R2 on chest wall). Due to the fact that the highest mediastinal lymph node was not routinely sent to pathology separately from the other nodes, we did not take the N factor into consideration to define an incomplete resection. All patients underwent a total and circumferential resection of bronchus. The anastomosis was performed with whole layer interrupted suturing, first with silk, later alternating silk with chromic catgut and then with Vicryl® or PDS®. The anastomosis was routinely covered with a pedicled parietal pleura flap or parietal pleura flap. Two patients underwent sleeve lobectomy after induction chemotherapy.

Operative mortality (OM) was taken to include 30 day mortality, all in-hospital mortality beyond 30 days, and mortality at home due to a cause strictly related to the operation, e.g. massive haemorrhage due to bronchovascular fistula. Most patients with pN2 disease underwent radiation therapy on the mediastinum if this was not contraindicated by the respiratory function. The revised TNM staging system was used to stage all patients [5].

Patients were followed up from the date of the operation to the time of death or to the end of observation (December 1999). For patients who were not routinely followed up, data were obtained by personal contact or by contact with the family doctor or relatives. The precise cause of death was not clear in all patients; when it was related to the lung cancer, sometimes it was not clear whether the site of recurrence was local, distant or both. One hundred and fifty-nine patients were evaluated for long-term survival (for statistical analysis, patients lost at follow-up were considered censored), and one patient was excluded because before lung resection she had been treated with radiosurgery for a brain metastasis.

Results are presented as percentages for categorical data. The X² test was used to compare these proportions. The analysis of survival was based on deaths from all causes including OM and data were evaluated separately for NSCLC and carcinoid tumors. Survival curves were obtained according to the Kaplan–Meier actuarial method and the log–rank test was used to compare survivals. A P value of less than 0.05 was considered significant. Univariate and multivariate analyses were used to identify factors that significantly influenced OM and mortality related to early bronchial anastomosis complications (dehiscence and bronchovascular fistula) in NSCLC patients and for this purpose the series was split into an early (up to 1993) and a contemporary phase (1994–1999). Variables entered into the model were age, stage, N status, functional status and microscopic residual disease on the bronchus (only for the appearance of early anastomotic complications and related mortality).

3. Results

The rate of resection increased from 2.2% of all operation performed for NSCLC and low-grade malignancies in the first 10 years of our experience to 4.7% of the last 10 years.

Histological examination showed a squamous cell carcinoma in 120 patients, a non-squamous cell carcinoma in 31 patients (adenocarcinoma 27, large cell carcinoma 2, adenosquamous carcinoma 2) and a typical carcinoid in nine patients. According to pTNM classification there were five patients in stage IA, 52 in stage IB, four in stage IIA, 48 in stage IIb, 45 in stage IIIA, five in stage IIIB and one in stage IV. In stage I patients there were 47 squamous cell carcinoma, nine carcinoids and one adenocarcinoma, in stage II 33 squamous cell and 18 non-squamous cell carcinomas, in stage III 40 squamous cell and 11 non-squamous cell carcinomas, in stage IV one adenocarcinoma. Twelve patients were lost at follow-up after a mean time of 39 months.

3.1. Results of sleeve lobectomy for NSCLC, early phase

OM was 14.6% (15/103 patients). Causes of death were bronchopleural fistula in eight cases, bronchovascular fistula in two cases, cardiac in three cases and other in two cases. Mortality rates by age, functional status, stage and N were
the following. In patients aged 70 or over mortality was 36% (9/25) while in patients under 70 years it was 7.7% (6/78). In functionally compromised patients the mortality rate was 29% (8/27) while in non-compromised patients it was 9.2% (7/76). Mortality by stage was 8.8% in stage I (3/34), 13.8% in stage II (5/36) and 21% in stage III (7/33); in N0 patients mortality was 14% (6/43), in N1 it was 6% (2/33) and in N2 patients it was 23% (7/30). Univariate analysis did not detect any significant difference in mortality in relation to stage or to N (P = NS) but mortality was significantly higher in patients aged 70 or older compared to patients under 70 (P < 0.001), and in patients who were functionally compromised compared with non-compromised patients (P = 0.02). Again mortality related to early anastomotic complications was significantly higher in patients aged 70 or over (P = 0.02) but in functionally compromised patients the difference failed to reach significance, while no statistically significant difference was detected among stages or N groups (Table 1).

Multiple logistic regression analysis revealed that age (P = 0.008), but not pN factor, stage and functional status, had a significant influence on OM. When the age variable was removed, functional status (P = 0.05) was the only factor significantly influencing the mortality rate. Age and positive bronchial margins had a significant influence on mortality related to early anastomotic complications (P = 0.05) and again when the age variable was removed, functional status and positive bronchial margins were the factors significantly influencing the mortality related to early anastomotic complications. Non-fatal complications occurred in 16 patients (14.5%); they comprised lobar atelectasis in eight patients, prolonged air leaks in two patients, atrial fibrillation in six patients, chylothorax in one patient, non-fatal bronchopleural fistula in two patients and postoperative bleeding in two patients; in a few patients more than one complication occurred. Bronchopleural fistula either fatal or not occurred in eight patients with N2 disease, in two with N1 disease and in two with N0 disease. Late stenosis occurred in eight completely resected patients (7.7%), three on the left side and five on the right side; stenoses appeared in most cases within 3 months from operation (six cases) and when silk was used as a suturing material due to granulation tissue formation (five cases), the other two cases appeared after 6 and 9 months. All the three left-sided cases required a completion pneumonectomy, the other five required endoscopic excision of bronchial suture granulomas; a completion pneumonectomy was also performed in five other patients for a dehiscence as a salvage procedure (three died and two survived) or for local recurrence in one case.

### 3.2. Results of sleeve lobectomy for NSCLC, contemporary phase

OM was 6% (3/48). Causes of death were bronchopleural fistula, bronchovascular fistula and pulmonary embolism. Mortality by age, functional status, stage and N were the following. In patients aged 70 or over mortality was 15% (2/13) while in patients under 70 years it was 3% (1/35). In functionally compromised patients mortality was 11% (1/9) while in non-compromised ones it was 5% (2/39). Mortality by stage was 7% in stage I (1/14), 6.2% in stage II (1/16) and 5.9% in stage III (1/17), 0% in stage IV (0/1); in N0 patients mortality was 11.7% (2/17), in N1 it was 5.5% (1/18) and in N2 it was 0% (0/13). Univariate analysis did not detect any significant difference in mortality in relation to stage, N, age or functional status (P = NS). Again no significant difference was detected for mortality related to early anastomotic complications. Multiple logistic regression analysis was not able to detect any factor significantly influencing OM or mortality related to early anastomotic complications. Non-fatal complications occurred in five patients and there was stroke and wound infection in one patient each and atrial fibrillation in three patients. Late stenosis occurred in one completely resected patient 4 months after a right upper sleeve lobectomy and was treated by dilatation and positioning of a Wallstent.

### Table 1
Causes of mortality by age, stage, compromised/non-compromised patients and N factor in the early phase

<table>
<thead>
<tr>
<th>Age</th>
<th>BP fistula</th>
<th>BV fistula</th>
<th>Cardiac</th>
<th>Other</th>
<th>Global</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age &gt;70</td>
<td>5</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>9/25 (36%)</td>
<td>P &lt; 0.001</td>
</tr>
<tr>
<td>Age &lt;70</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>6/76 (7.7%)</td>
<td></td>
</tr>
<tr>
<td>Stage IAB</td>
<td>1</td>
<td>/</td>
<td>1</td>
<td>1</td>
<td>3/34 (8.8%)</td>
<td>P = NS</td>
</tr>
<tr>
<td>Stage IIAB</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>/</td>
<td>5/36 (13.8%)</td>
<td></td>
</tr>
<tr>
<td>Stage IIIAB</td>
<td>4</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>7/33 (21%)</td>
<td></td>
</tr>
<tr>
<td>Comp.*</td>
<td>5</td>
<td>1</td>
<td>/</td>
<td>2</td>
<td>8/27 (29%)</td>
<td></td>
</tr>
<tr>
<td>Non-comp.</td>
<td>3</td>
<td>1</td>
<td>3</td>
<td>1</td>
<td>7/76 (9.2%)</td>
<td>P = 0.02</td>
</tr>
<tr>
<td>N0</td>
<td>2</td>
<td>/</td>
<td>3</td>
<td>1</td>
<td>6/43 (14%)</td>
<td></td>
</tr>
<tr>
<td>N1</td>
<td>1</td>
<td>1</td>
<td>/</td>
<td>/</td>
<td>2/33 (6%)</td>
<td>P = NS</td>
</tr>
<tr>
<td>N2</td>
<td>5</td>
<td>1</td>
<td>/</td>
<td>1</td>
<td>7/30 (23%)</td>
<td></td>
</tr>
</tbody>
</table>

* Comp., functionally compromised patients and/or comorbidity factors.
3. Carcinoids

Nine patients underwent a sleeve lobectomy for a typical carcinoid tumor. Their mean age was 39 years (SD 13.3). OM and postoperative complications were nil although operative technique was identical to that used for NSCLC including mediastinal nodes dissection due to the fact that typical and atypical carcinoids cannot be usually identified preoperatively on small biopsy specimens obtained by bronchoscopy. No late stenosis occurred.

The actuarial survival rate was calculated excluding carcinoids (nine cases) and the stage IV patients; for 150 patients it was 51.3% after 3 years, 38.8% after 5 years and 20.5% after 10 years, while for carcinoids it was 100%. Three, 5 and 10-year survival rates for stage I(A–B) were 77, 62 and 31%, for stage II(A–B) 45, 34 and 27% and for stage III(A–B) 33, 22 and 0%. There was no significant difference at log–rank test between stages II and III while the difference among stages I and II and III was highly significant \(P = 0.001\) (Fig. 1). When survival was analyzed in relation to nodal status, 3, 5 and 10-year survival rates were 71, 57 and 33% for N0 disease, 42, 33 and 22% for N1 disease and 34 and 19% for N2 disease with the last observation of 19% at 82 months. There was no significant difference in survival between N1 and N2 disease but a significant difference was found among N0 and N1 and N2 disease \(P < 0.001\); however, survival curves show a more favorable trend for N1 versus N2 disease and for stage II versus stage III disease (Figs. 1–2). The 5 and 10-year survival rate for carcinoids was 100%. Three out of the seven patients with R1-2 disease are alive, two after radiation therapy and one after completion pneumonectomy. Six patients (4%) had a second primary lung cancer which was resected.

So far 97 out of 160 patients (61%) have died, 25 in stage I, 32 in stage II and 40 in stage III; follow-up data were detailed for 76 of these patients. The causes of death were as follows: for stage I disease (24 patients) local recurrence in four (16.5%), local and distant in two (8%), distant only in four (16.5%) and other than lung cancer in 14 (58%); for stage II disease (20 patients) local recurrence in two (10%), local and distant in six (30%), distant only in nine (45%) and other than lung cancer in three (15%); for stage III disease (32 patients) local recurrence in two (6%), local and distant in ten (31%), distant only in 14 (44%) and other than lung cancer in six (19%).

4. Discussion

Bronchoplastic procedures have been judged to be appropriate for 5–8% of patients with NSCLC [4] and in some case series they make up a proportion as high as 19% [6], although sleeve lobectomies constituted about 4% of lung resections performed for NSCLC in our Division and its percentage increased from 2.2 to 4.7%. A sleeve lobectomy has the same functional result of a standard lobectomy although it takes 3–4 months after surgery for the reimplanted lung lobe to reach a complete recovery and substantially contribute to residual postoperative pulmonary function [3]. Sleeve lobectomies, particularly useful in patients with a limited respiratory reserve, in elderly patients or patients with associated comorbid diseases (metabolic, cardiovascular, neurological, renal or hepatic) for whom a pneumonectomy would be hazardous are also valuable for patients who are capable of tolerating a pneumonectomy, as was the case in most of our patients, in that it allows a better quality of life and further lung resection. A second resection for a second primary lung cancer was necessary in six of our patients (3.8%), which is half the percentage reported by Van Schil et al. [7] (7.6%). This difference might be explained by the higher percentage of patients in stage I in Van Schil et al. group; more patients in stage I disease means more patients who can develop a second primary lung cancer due to longer survival. Although a lung resection can be performed on a single lung after pneumonectomy [8,9], a second lung resection can be more safely performed in patients who underwent sleeve lobectomy compared with patients who had a pneumonectomy. Similarly, there is no question that a better quality of life is achieved using a lung-sparing procedure, even if according to Ferguson and Karrison [10], long-term survival is not significantly influenced by pneumonectomy compared with lesser resection. The OM rate, which usually refers to mortality within 30 postoperative days is 5.5% after sleeve lobectomies according to Tedder et al. [4], although it can range from 0 to 12% [11,12] and even up to 36% [13]. In
our experience, all in-hospital mortality and mortality for reasons related to the operation (two patients died after 30 days at home due to massive haemoptoe and one from PE) for NSCLC was 14.6% in the early phase but it decreased to 6% in the contemporary one.

Although the importance of the learning curve cannot be underestimated, neither the suturing technique nor the suturing material have changed since the beginning of the 1980s, and maneuvers to obtain a tension-free anastomosis were always applied when required. OM declined first of all due to improved patient selection and the effort to avoid excessive devascularization by preserving peribronchial vascular tissue in the areas adjacent to the anastomotic sites helped to reduce problems to the anastomosis site with its consequence in terms of mortality and late stenoses. Careful preoperative assessment is crucial; although some authors do not report a higher mortality in patients who are functionally compromised, this was our experience at least in our earlier experience and was also reported by Weisel et al. [14]. It is interesting to note that a low mortality rate was reported in groups of patients with a low percentage of functionally compromised patients and/or N2 patients [15], and this further supports the importance of careful patient selection. Icard et al. [16] reported that no difference in mortality was found between compromised and non-compromised patients, although 41% of their patients were compromised patients, but in most of them a large wedge resection was performed instead of a full bronchial sleeve resection; it may be supposed that preserving a small area of bronchial vascularization may help to avoid bronchial dehiscence and the related high mortality in compromised patients (seven out of nine in our experience).

Since 1994 we have adopted the algorithm proposed by Marshall and Olsen [17] to identify patients at high risk; if patients at risk have comorbidity factors (poor nutritional status, liver or kidney disease, diabetes, cardiac disease, peripheral vascular disease or previous stroke) and are aged 70 or over we very carefully consider that patient for bronchoplastic surgery. We did not consider clinical N2 disease a contraindication to sleeve lobectomy, but in the past few years we have avoided surgery in patients with clinical N2 who are aged 70 or over and are functionally compromised or have other comorbidity factors; in the other cases of clinical N2 disease, we performed resection after induction chemotherapy.

Bronchovascular and bronchopleural fistulas occurred globally in 7.5% of our patients, a proportion in line with current data. The related mortality was very high in our experience as well as in that reported by others [18,19]; unfortunately, it is not clear whether the high mortality rate reported occurred in compromised patients, as in our case series.

Late stenosis occurred in 7.7% of our patients in the early phase and were related in most cases to granulation tissue formation due to the use of silk as suturing material and occurred only in 2% of cases in the contemporary series of sleeve lobectomies. Stenoses were treated endoscopically by removing granulation tissue and suturing material, by the placement of a stent, or by completion pneumonectomy when the remaining lobe was too damaged or the stenosis was so tight as not to allow the placement of a stent and this happened always on the left side where bronchial calibre is reduced. The actuarial survival rate was in line with data reported by Mountain [5] for the same stage. It should be noted that we considered stages including stages A and B, that is stage IA–B, IIA–B and IIIA–B because the number of patients in some subgroups (that is IA, IIA and IIIB) was quite small. The actuarial survival rate was obtained by excluding patients with carcinoids, for whom the survival rate was 100% at 5 and 10 years, thus confirming Schepens et al.’s [20] report on late results of sleeve resection for typical bronchial carcinoids.

The cause of death in most cases was local/distant or distant recurrence in patients with stage II or III disease while most patients in stage I died of causes other than lung cancer. These data are in contrast with those reported by Tronc et al. [15] but are similar to those reported by Van Schil et al. [21], who showed that most patients with N1–N2 disease who underwent sleeve lobectomy died due to distant metastases. A significant difference between stages was found when stage I was compared to stages II and III (P < 0.05) but not when stage II was compared with stage III (P = NS).

In conclusion, sleeve lobectomy is a valid alternative to pneumonectomy and leads to better postoperative pulmonary function without any decrease in long-term survival. Careful patient selection makes it possible to achieve an OM rate comparable to or lower than that of pneumonectomy; the benefit of this procedure in terms of quality of life is difficult to measure but is surely appreciated by the patient.

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